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Serum leptin concentration and anaerobic performance do not change during the menstrual cycle of young females

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Abstract

OBJECTIVES: It was aimed to determine whether there was a difference in the leptin levels and short term exercise performance during the menstrual cycle of the young females who had normal menstrual cycle and no pregnancy story.
SETTING AND DESIGN: Fifteen sedentary females aged 19–23 yrs were included. All had regular menstrual cycle of 28–30 days and no pregnancy story. Blood samples were taken for the analysis of serum estradiol, progesterone and leptin levels and Wingate test was applied on a Monark 818E ergometer with 75 g/kg load on the 7th, 14th and 21st cycle days, randomly.
RESULTS: The differences in serum leptin levels and peak power, mean power and fatigue index during these days and the correlations between serum leptin and FSH, LH, estradiol and progesterone levels were not significant.
CONCLUSIONS: We concluded that performance in a short intense exercise which require high motivation is not affected by menstrual cycle and in young females with normal menstrual cycle, serum leptin concentration does not change during the cycle. Further studies constituting more standard groups, controlling food intake, timing the blood sampling, studying more days of menstrual cycle will help to obtain more accurate results.

Introduction

The presence of leptin is required for proper reproductive function and leptin is a signal to the reproductive axis [31]. Information on body fat stores may be transferred to the reproductive organs through leptin. While the mechanism by which leptin affects reproductive function is not yet fully understood, the evidence suggests that its effects can be mediated both centrally and peripherally. Leptin receptors have been identified in hypothalamus, gonadotrope cells of the anterior pituitary, [14] granulose, theca and interstitial cells of ovary [16] and endometrium [17]. Leptin is present in follicular fluid and can induce a biological response in ovarian cells, suggesting that leptin may have a direct effect on human ovary [16]. Leptin may regulate the minute-to-minute oscillations in the levels of LH and estradiol [21].

Reports on the relationship between leptin and ovarian steroids have been conflicting. Progesterone had no effect on leptin secretion, estrogen selectively increased leptin secretion from adipocytes obtained from women, but not men [2]. In menstrual cycles those were superovulated with FSH, resulting in a continuous rise in estradiol to the levels exceeding physiological values, there was no effect of estradiol on leptin secretion, which suggests there may be a limit to the stimulatory effect of estradiol on leptin secre-

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tion [28]. Since oral contraceptive steroids induce a pharmacological rather than a physiological state, the relationship between leptin and contraceptive steroids may be unlike to the one between leptin and ovarian sex hormones at various phases of menstrual cycle [40].

In humans, leptin levels exhibit significant changes during progressive pubertal stages, with a distinct dimorphism between boys and girls. Serum leptin levels in boys appear to peak just before puberty or in early Tanner stages, followed by a decrease as testosterone levels rise [24,1,7,13]. Girls, on the other hand, display a steady rise in leptin levels throughout puberty [1,7,13]. In addition, a significant relationship exists between the onset of menarche and serum leptin levels, with an increase of 1 ng/ml in serum leptin levels associated with an earlier onset of menarche by 1 month [26].

Although some studies [34,33] showed that serum leptin levels declined in postmenopausal women, especially in obese ones, probably due to altered sex steroid levels in postmenopausal state. Others [10,3,9] reported that leptin concentrations in postmenopausal women receiving hormone replacement therapy were similar to those in untreated post- and premenopausal women, suggesting neither natural menopause nor estrogen affects leptin levels.

The possible variation of serum leptin levels during the different phases of the menstrual cycle has been studied and controversial results have been obtained [34,12,35,32,39,38,23].

The recent increase in participation of women in recreational activity has led to an increased interest in the physiology of exercising females. Exercise-associated reproductive dysfunction, such as amenorrhea and luteal phase defects, is prevalent in female athletes [22]. Increasing evidence supports the notion that these menstrual disturbances are related to exercise-induced negative energy balance resulting from insufficient energy intake to compensate for the energy cost of exercise [19]. However, the underlying mechanism of the menstrual disturbances in these athletes remains unclear.

The purpose of the present study was to investigate whether there was a difference in the leptin levels and anaerobic performance during the normal menstrual cycle.

Materials and methods

Fifteen sedentary females aged 19–23 yrs volunteered. The subjects had never smoked, used no medication (including oral contraceptives) for 3 months and had no pregnancy story before the study and none of them was obese. All had regular menstrual cycle of 28–30 days. The protocol was approved by the local ethical committee. All participants gave a written informed consent after full explanation of the purpose and nature of all procedures used. Blood samples were taken for the analysis of serum estradiol, progesterone and leptin levels at the same hours (10 am) on the 7^{th}, 14^{th} and 21^{st} cycle days randomly. The sex hormones were determined using Immulite 2000 chemiluminescent immunoassay kit, and the leptin was determined with IRMA DSL 23100 (Diagnostic System Laboratories, Inc, Webster, TX) using human leptin radioimmunoassay kit. The lower limit of sensitivity for leptin was 0.5 ng/ml. The intraassay coefficient of variation of the assay at 30 μg/L was 3.9%, at 12 μg/L 1.7%. The results of 3 subjects whose progesterone levels were under 2 ng/ml during the midluteal period were excluded.

Body weight and percent body fat were measured by bioimpedance meter (Tanita). After blood samples were taken, the Wingate test of 30-sec was applied on a Monark 818E ergometer with 75 g/kg load. The subjects were provided with the same conditions on different periods of menstrual cycle by recording the seat height for them. After the subjects were familiarized with the ergometer, they were asked to pedal for 4–5 sec as fast as possible and when they reached sufficient speed, the predetermined load was applied. Pedal rotations were counted by an electronic counter with resolution of 1/12 revolution and power output was calculated for each 5-sec. Peak power, mean power, fatigue index for each Wingate test were computed.

All data are presented as mean ± SD. The differences between measurements were evaluated with one-way analysis of variance. Pearson's Product moment correlation coefficients were used for investigating relationship between the variables. The significance level was determined as $p < 0.05$.

Results

The differences between serum leptin levels on the 7^{th}, 14^{th} and 21^{st} cycle days were not significant (*Table I*). There was no difference between the peak power, mean power and fatigue index calculated in three different phases of the menstrual cycle.

The correlation coefficients between serum leptin and serum FSH, LH, estradiol, progesterone levels and mean power, peak power and fatigue index were not significant (*Table II*).

Discussion

Hardie et al [12] reported that changes in circulating leptin levels in 9 women were associated with the menstrual phase and that peak leptin concentrations were recorded during the luteal phase, coincident with elevation of serum progesterone levels. Ludwig et al [23] and Riad-Gabriel et al [32] have shown considerable variation in leptin levels throughout the menstrual cycle, with higher levels in midluteal rather than the follicular phase. Shimizu et al [34] found serum leptin to have been slightly higher during the luteal than during the follicular phase of the cycle, although there was no difference in total body fat in two periods. Thong et al [39] found a 40–46% rise in leptin during the luteal phase of the menstrual cycle in 8 elite female athletes. However, the absolute rise in leptin in midluteal phase was much smaller and was not consistently found in all the cyclic athletes [39].

Table I: The mean (± SD) values obtained on the 7th, 14th and 21st days of the menstrual cycle.

	7th day	14th day	21st day
Leptin (ng/ml)	29.2 ± 8.9	31.4 ± 9.0	32.0 ± 9.2
Body weight (kg)	60.3 ± 8.4	60.2 ± 8.0	60.8 ± 8.1
Percent body fat	27.4 ± 5.9	27.8 ± 5.8	28.0 ± 5.6
Body mass index (kg/m^2)	22.5 ± 2.2	22.5 ± 2.1	22.7 ± 2.1
Mean power (watt)	278.8 ± 46.9	281.6 ± 44.2	277.6 ± 46.6
Peak power (watt)	401.3 ± 76.7	419.3 ± 86.6	414.6 ± 87.8
Fatigue index (%)	51.8 ± 9.2	51.2 ± 12.6	51.8 ± 8.2
Estradiol (pg/ml)	56.2 ± 35.0	155.5 ± 92.4	119.3 ± 47.6
Progestrone (ng/ml)	0.49 ± 0.23	2.22 ± 2.85	8.61 ± 5.07
FSH (ng/ml)	5.93 ± 1.71	9.53 ± 5.14	3.12 ± 1.41
LH (ng/ml)	4.63 ± 1.38	28.36 ± 17.58	3.79 ± 2.12

Table II: Correlation coefficients between serum leptin and other variables on corresponding days.

	7th day	14th day	21st day
FSH	–0.200	0.109	–0.455
LH	0.049	0.400	–0.462
Estradiol	0.028	0.023	0.420
Progesterone	0.263	–0.191	0.126
Mean power	–0.280	–0.189	–0.014
Peak power	0.098	–0.301	0.210
Fatigue index	0.413	–0.266	0.126

For all $p > 0.05$

Stock et al [35] found a small overall variation in leptin levels during the menstrual cycle but when the phases were compared with each other, no statistically significant differences were obtained. Teirmaa et al [38] found that in 8 women with normal menstrual cycle and no hormonal therapy, serum leptin concentration were similar at the beginning of cycle, around the time of the anticipate ovulation and at the end of the cycle.

Since different results were reported about leptin levels during the menstrual cycle and it was not stated whether the participants had or not pregnancy in the studies, we aimed to study the leptin levels of the young females who had no pregnancy story.

Although the physiological significance of a rise in leptin in the luteal phase is unclear, it may be related to the fact that leptin may have a role in preparing the body for the metabolic demands of pregnancy [13]. While several studies reported a rise in the luteal phase, we found no difference in the leptin levels during the luteal phase as in the Tataranni et al's study [37] and this suggests that leptin does not have a role in preparing the body for pregnancy. For these reasons, the increase in leptin during the midluteal phase can be related to the fact that food intake increases during the luteal phase. Plasma leptin has been shown to increase with acute overfeeding [18].

In the present study performed on a group similar to their group (age, BMI), we obtained results supporting those of Teirmaa et al [38]. Leptin secretion exhibits a circadian pattern, serum concentrations steadily increasing from a nadir in the morning to peak concentrations after midnight [19]. Therefore, the timing of the blood sampling is a critical issue. We concluded that constituting more standard groups (investigating age and amount of the pregnancy, equalizing percent body fat between groups), especially controlling food intake, timing the blood sampling, studying more days of menstrual cycle will help to obtain clearer results.

Although several researchers have studied the effect of the menstrual cycle on exercise performance, there are few well controlled studies [5]. Few studies have described the performance during the short-term anaerobic tests through the menstrual cycle phases, and existing data are conflicting, possibly because of the method of cycle phase determination.

Parish and Jakeman [30] demonstrated that mean power output and peak power output during a modified Wingate test were greater in midfollicular phase than in midluteal days. Masterson [25] found that power performance in a Wingate test was higher during the luteal phase in fairly active females. De Bruyn-Prevost et al [4] and Doolittle and Engebretsen [6] failed to show any significant menstrual phase effects in anaerobic performance during a cycle ergometer test and a 600-yd run test. However, De Bruyn-Prevost et al [4] did not use any hormonal analysis of cycle phases and Doolittle and Engebretsen [6] took blood samples only in postexercise conditions. We did not observe any significant change in the anaerobic performance during the menstrual cycle which was confirmed by serum estradiol and progesterone assays. Lebrun et al [20] found that although both absolute and relative VO_{2max} were slightly lower during the luteal phase of the menstrual cycle in female athletes, there was no significant effect of menstrual cycle phase on the anaerobic performance, aerobic endurance performance, or isokinetic muscle strength. Giacomoni et al [8] failed to determine any influence of an ovulatory ovarian cycle on maximal anaerobic performance during cycling and jumping. Sunderland and Nevill [36] reported that for unacclimatised games players the performance of intermittent, high-intensity shuttle running in the heat was unaffected by menstrual cycle phase.

In the exercises of short duration, energy is supplied mainly by muscle phosphates and anaerobic glycolysis. Nicklas et al [29] found that glycogen repletion and consequently muscle glycogen content was greater during the luteal phase and that the rate of glycogen utilization during exhaustive exercise did not vary significantly between the follicular and luteal phases. Jurkowski et al [15] and McCracken et al [27] stated that the changes in blood lactate responses to exercise were affected by the phase of the menstrual cycle. The influence of menstrual cycle phase on muscle phosphate utilization in humans has not yet been studied. However, Harber et al [11] reported that amenorrheic endurance athletes had slower CP recovery rates, following plantar flexion exercises, than their eumenorrheic counterparts, suggesting an influence of ovarian hormone status on muscle phosphate recovery.

We concluded that; 1) Performance in a short-term intense exercise which require high motivation is not affected by menstrual cycle period, 2) In young females with normal menstrual cycle and no hormonal therapy, serum leptin concentration does not change throughout the cycle, 3) Constituting more standard groups, controlling food intake, timing the blood sampling, studying more days of menstrual cycle will help to obtain clearer results.

REFERENCES

1 Blum WF, Englaro P, Hanitsch S, Juul A, Hertel NT, Müller J, et al. Plasma leptin levels in healthy children and adolescents: Dependence on body mass index, body fat mass, gender, pubertal state, and testosterone. J Clin Endocr Metab 1997; **82**:2904–2910.

2 Casabiell X, Pineiro V, Peino R, Lage M, Camina J, Gallego R, et al. Gender differences in both spontaneous and stimulated leptin secretion by human omental adipose tissue in vitro: Dexamethasone and estradiol stimulate leptin release in women, but not in men. J Clin Endocr Metab 1998; **83**:2149–2155.

3 Castracane VD, Kraemer RR, Franken MA, Kraemer GR, Gimpel T. Serum leptin concentration in women: Effect of age, obesity, and estrogen administration. Fertil Steril 1998; **70**:472–477.

4 De Bruyn-Prevost P, Masset C, Sturbois X. Physiological response from 18–25 years women to aerobic and anaerobic physical fitness tests at different periods during the menstrual cycle. J Sports Med 1984; **24**:144–148.

5 De Souza MJ, Maguire MS, Rubin KR, Maresh CM. Effects of menstrual phase and amenorrhea on exercise performance in runners. Med Sci Sports Exerc 1990; **22**:575–580.

6 Doolitle TL, Engebretsen J. Performance variations during the menstrual cycle. J Sports Med 1972; **12**: 54–58.

7 Garcia-Mayor RV, Andrade MA, Rios M, Lage M, Dieguez C, Casanueva FF. Serum leptin levels in normal children: Relationship to age, gender, body mass index, pituitary-gonadal hormones, and pubertal stage. J Sports Med 1997; **82**:2849–2855.

8 Giacomoni M, Bernard T, Gavarry O, Altare S, Falgairette G. Influence of the menstrual cycle phase and menstrual symptoms on maximal anaerobic performance. Med Sci Sports Exerc 2000; **32**:486–492.

9 Hadji P, Görke K, Hars O, Bauer T, Emons G, Schulz K. The influence of hormone replacement therapy (HRT) on serum leptin concentration in postmenopausal women. Maturitas 2000; **37**:105–111.

10 Haffner SM, Mykkänen L, Stern MP. Leptin concentrations in women in the San Antonio Heart Study: Effect of menopausal status and postmenopausal hormone replacement therapy. Am J Epidemiol 1997; **146**:581–585.

11 Harber VJ, Petersen SR, Chilibeck PD. Thyroid hormone concentrations and muscle metabolism in amenorrheic and eumenorrheic athletes. Can J Sports Med 1998; **23**:293–306.

12 Hardie L, Trayhurn P, Abramovich D, Fowler P. Circulating leptin in women: A longitudinal study in the menstrual cycle and during pregnancy. Clin Endocrinol 1997; **47**:101–106.

13 Horlick MB, Rosenbaum M, Nicolson M, Levine LS, Fedun B, Wang J, et al. Effect of puberty on the relationship between circulating leptin and body composition. J Clin Endocr Metab 2000; **85**:2509–2518.

14 Jin L, Zhang S, Burguera BG, Couce ME, Osamura RY, Kulig E, et al. Leptin and leptin receptor expression in rat and mouse pituitary cells. Endocrinology 2000; **141**:333–339.

15 Jurkowski JEH, Jones NL, Toews CJ, Sutton JR. Effects of menstrual cycle on blood lactate O_2 delivery, and performance during exercise. J Sports Med 1981; **51**:1493–1499.

16 Karlsson C, Lindell K, Svensson E, Bergh C, Lind P, Billig H, et al. Expression of functional leptin receptors in the human ovary. J Clin Endocr Metab 1997; **82**:4144–4148.

17 Kitawaki J, Koshiba H, Ishihara H, Kusuki I, Tsukamoto K, Honjo H. Expression of leptin receptor in human endometrium and fluctuation during the menstrual cycle. J Clin Endocr Metab 2000; **85**:1946–1950.

18 Kolaczynski JW, Ohannesian JP, Considine RV, Marco CC, Caro JF. Response of leptin to short-term and prolonged overfeeding in humans. J Clin Endocr Metab 1996; **81**:4162–4165.

19 Laughlin GA, Yen SSC. Nutritional and endocrine-metabolic aberrations in amenorrheic athletes. J Clin Endocr Metab 1996; **81**:301–4309.

20 Lebrun CM, McKenzie JC, Prior JC, Taunton JE. Effects of menstrual cycle phase on athletic performance. Med Sci Sports Exerc 1995; **27**:437–444.

21 Licinio J, Negrao AB, Mantzoros C, Kaklamani V, Wong M, Bongiorno PB, et al. Synchronicity of frequently sampled, 24-h concentrations of circulating leptin, luteinizing hormone, and estradiol in healthy women. Proc Natl Acad Sci 1998; **95**:2541–2546.

22 Loucks AB, Mortola JF, Girton L. Yen SSC. Alterations in the hypothalamic-pituitary-adrenal axes in athletic women. J Clin Endocr Metab 1989; **68**:402–411.

23 Ludwig M, Klein HH, Diedrich K, Ortman O. Serum leptin concentrations throughout the menstrual cycle. Arch Gyn Obstet 2000; **263**:99–101.

24 Mantzoros CS, Flier J, Rogol AD. A longitudinal assessment of hormonal and physical alterations during normal puberty in boys. V. Rising leptin levels may signal the onset of puberty. J Clin Endocr Metab 1997; **82**:1066–1070.

25 Masterson G. The impact of menstrual phases on anaerobic power performance in collegiate women. J Streng Condition Res 1999; **13**:325–329.

26 Matkovic V, Ilich JZ, Skugor M, Badenhop NE, Goel P, Clairmont A, et al. Leptin is inversely related to age at menarche in human females. J Clin Endocr Metab 1997; **82**:3239–3245.

27 McCracken M, Ainsworth B, Hackney AC. Effects of the menstrual cycle phase on the blood lactate responses to exercise. Eur J Appl Physiol 1994; **69**:174–175.

28 Messinis IE, Milingos S, Zikipoulos K, Kollios G, Seferiadis K, Lolis D. Leptin concentrations in the follicular phase of spontaneous cycle and cycles superovulated with follicle stimulating hormone. Hum Reproduc 1998; **13**:1152–1156.

29 Nicklas BJ, Hackney AC, Sharp RL. The menstrual cycle and exercise: Performance, muscle glycogen, and substrate responses. Int J Sports Med 1989; **10**:264–269.

30 Parish HC, Jakeman PM. The effects of menstruation upon repeated maximal sprint performance. J Sports Sci Med 1987;1:78.

31 Rechberger T, Baranowski W, Postawski K, Jakimiuk AJ, Tomaszewski J, Kulik-Rechberger B, et al. Serum leptin concentrations in women taking oral contraceptives. Eur J Obstet Gynecol Reproduc Biol 1999; **83**:105–108.

32 Riad-Gabriel MG, Jinagouda SD, Sharma A, Boyadjian R, Saad MF. Changes in plasma leptin during the menstrual cycle. Eur J Endocrinol 1998; **139**:528–531.

33 Rosenbaum M, Nicolson M, Hirsch J, Heymsfield SB, Gallagher D, Chu F, et al. Effects of gender, body composition, and menopause on plasma concentrations of leptin. J Clin Endocr Metab 1996; **81**:3424–3427.

34 Shimizu H, Shimomura Y, Nakanishi Y, Futawatari T, Ohtani K, Sato N, et al. Estrogen increases in vivo leptin production in rats and human subjects. J Endocr 1997; **154**:285–292.

35 Stock SM, Sande EM, Bremme KA. Leptin levels vary significantly during the menstrual cycle, pregnancy, and in vitro fertilization treatment: Possible relation to estradiol. Fertil Steril 1999; **72**:657–662.

36 Sunderland C, Nevill M. Effect of the menstrual cycle on performance of intermittent, high-intensity shuttle running in a hot environment. Eur J Appl Physiol 2003; **88**:345–352.

37 Tataranni PA, Monreo MB, Dueck CA. Adiposity, plasma concentration and reproductive function in active and sedentary females. Int J Obesity 1997; **21**:818–821.

38 Teirmaa T, Luukkaa V, Rouru J, Koulu M, Huupponen R. Correlation between circulating leptin and luteinizing hormone during the menstrual cycle in normal-weight women. Eur J Endocrinol 1998; **139**:190–194.

39 Thong FSL, McLean C, Graham TE. Plasma leptin in female athletes: Relationship with body fat, reproductive, nutritional, and endocrine factors. J Appl Physiol 2000; **88**:2037–2044.

40 Watanabe RM, Azen CG, Roy S, Perlman JA, Bergman RN. Defects in carbohydrate metabolism in oral contraceptive users without apparent metabolic risk factors. J Clin Endocr Metab 1994; **79**:1277–1283.